REMARKS/ARGUMENTS

THE INVENTION

This invention provides for an efficient and economic means to differentially diagnose prostate cancer from benign prostate hyperplasia (BPH) by looking at differences in low molecular protein markers using mass spectroscopy.

STATUS OF THE CLAIMS

Claims 1, 8, 12, 20, and 84-94 are pending. Claim 1 is amended to clarify that the method provides for the use of mass spectroscopy to distinguish between prostate cancer and benign hyperplasia by looking at a shift in the pattern of low molecular weight proteins rather than looking at specific markers. It being understood that the pattern (MS profile) is derived from a collection of markers; but, you do not need to identify them as specific markers.

Support for the amendments to claim 1 can be found on page 22 of the specification describing the way MS data can be analyzed and in Figures 3 and 6 depicting the gel views.

The pending claims are rejected under §112 first and second paragraphs and are provisionally rejected for double patenting.

Interview Summary

Pursuant to rule 133(b), applicants acknowledge with gratitude the Examiner's suggestions during a telephonic interview on February 21, 2007. Claim 1 was discussed with regard to the Examiner's suggestion that we limit our claims to specific markers. It was explained that the invention permits those of skill to distinguish between prostate cancer and benign hyperplasia by looking at a shift or increase in the pattern of low molecular weight proteins due to increased prostate-specific antigen (PSA) activity rather than by the presence or absence of specific markers. Although the pattern is derived from a collection of these markers, it was explained that one need not actually identify them as specific markers. No agreement as

to claims was reached and the amendments to the claim 1 as proposed above are intended to clarify this aspect of the invention.

REJECTIONS UNDER §112

Applicants acknowledge with appreciation the withdrawal of the previous rejections under §112 in view of Dr. Yip's Rule 132 Declaration.

Written Description

The Examiner has rejected the pending claims as failing to comply with the written description requirement. He writes:

> In the instant case, the claims are inclusive of a genus of markers…characterized by an apparent molecular weight of less than 10,000 Da which can be used as a diagnostic marker to discriminate between prostate cancer and benign prostate hyperplasia. However, the written description in this case only sets forth a representative number of species of peptide obtained from seminal plasma characterized by a molecular weight of 2776 DA, 4423 DA, 4480 Da, 5733, 6098 Da, 6270 Da, …

Accordingly, the Examiner has encouraged the inclusion of the various markers in the pending claims.

In response, applicants again explain that the invention is not merely the discovery of specific markers. The invention includes taking advantage of increased PSA activity in prostate cancer cells that generates an increase in undefined, low molecular weight protein markers. The presence of these markers produces a shift in the MS profile or pattern of proteins below 10kDa,

The following legal analysis explains that the Examiner's focus on "specific markers" is not appropriate here because the **inventive principle** underpinning the rejected claims does not require knowledge of specific markers. Thus, there is no legal requirement for applicants to set forth specific markers in the claims. Applicants urge that they only have to set forth specific markers if the invention required specific markers to be practiced.

The Examiner relies on various court decisions to support his rejection. The Examiner is first reminded of the Federal Circuit's admonition that description rejections are very fact dependent and that each case must be carefully reviewed on its merits. The *Vas-Cath* court states on page 1562 quoting the CCPA in the *Driscoll* decision:

> It should be readily apparent from recent decisions of this court involving the question of compliance with the description requirement of § 112 that each case must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited.
>
> *In re Driscoll, 562 F.2d 1245, 1250, 195 U.S.P.Q. 434, 438 (CCPA 1977).*

Let's look at the facts of the court decisions supporting the Examiner's rejections. In the cases relied upon by the Examiner, the inventors were claiming novel *things* and their invalid claims included *things* not in their possession, *things* not yet discovered and *things* not described. In the subject application. the claims read on a novel **method** of performing actions upon old and new *things* (proteins in a sample). Because the *things* (low kDa proteins) of our method claims are not the patentable feature, we need not possess all *things* to be granted method claims.

The pending claims are like a software program designed to correct spelling errors. We need not possess all existing and future English words to have a claim recite a step of comparing a user entered word against a dictionary of words. Accordingly, in the pending claims, we need not identify all the lower molecular weight proteins—at least when we are not claiming them as ours.

More specifically, in both *Vas-Cath* and *Fiddes*, the inventors were claiming things they had made. *Vas-Cath* had pictures of a catheter, the accused infringers were arguing that the pictures did not adequately describe the catheters of the claims. They lost that argument. In *Fiddes* and *Amgen*, the invalid claims broadly defined nucleic acids encoding any protein that was fibroblast growth factor or erythropoietin. Having no ability to describe all such proteins, these claims failed under both enablement and description.

Applicants are claiming novel "methods" and the final step in our logical progression is to distinguish between fact patterns when method claims can include novel, yet to be discovered things, and when method claims cannot claim so broadly. The case law is clear on this. The test is one of "**inventive principle**" as mentioned above. Where the patentable feature is the thing, you can't get method claims that include things beyond your possession; but where the patentable aspects of the claims reside outside the thing, broad protection is available. The following three cases illustrate this body of law relating to "inventive principle."

Of the three cases, *In re Lange*, 209 USPQ 288 (CCPA, 1981), is the most recent. In *Lange*, the invention related to the use of electronegative gases to coat electrical devices to dampen arcing (sparks). The Examiner noted that the claims were broad enough to read on casting of electrodes and that the disclosure was limited to coating of preexisting electrodes. Convinced that this single species was not easily obtainable, the Examiner refused to allow the claims due to over breadth.

In rejecting the position of the Patent Office, the CCPA noted that the invention is the use of the gases to dampen sparks. No claim was drawn to casted electrodes. The entire claims were allowed and the CCPA stated:

> However, although appellant can be required to limit his claims to that subject area which is adequately disclosed, the existence of species which are not adequately disclosed does not require that the entire application be found nonenabling. See In re Cook, 58 CCPA 1049, 439, F.2d 730, 169 USPQ 298 (1971). This is especially true in this case where, as stated by appellant at oral argument, the method of forming the electrodes is **not the inventive principle** [Emphasis added].

The other two cases are *In Application of Fuetterer*, 138 USPQ 217 (CCPA 1963) and *Application of Herschler*, 200 USPQ 711 (CCPA 1979). In *Fuetterer*, the applicant had discovered that the addition of a protein with an inorganic salt to the materials used to make tire tread increased the stopping ability of tires made from the materials. The Examiner in Fuetterer argued that the scope of the claims was too broad and the amount of experimentation required to successfully use undisclosed inorganic salts should require the applicant to restrict his claims to the disclosed salts. The CCPA reversed the breadth rejection, explaining that this invention was

the combination of inorganic salts with the other elements of the claims. The fact that novel inorganic salts might be developed later did not preclude broad claims to the inventive combination.

In *Herschler*, the applicant had discovered that dimethylsulfoxide (DMSO) was useful as a transdermal carrier for physiologically active steroids. The CCPA found that a priority application describing a single steroid (dexamethasone 21-phosphate) supported a claim to the genus of all steroids. Citing *Fuetterer*, the court explained that Herschler's claims were not drawn to a novel steroid but to the method of administration of steroids. As long as the class of steroids could be expected to be carried across the skin by DMSO, the claim could encompass any steroid, known or unknown. As in *Fuetterer*, the CCPA reminded the Patent Office that the inventive principle was a method of administration of steroids and that the specific steroid exemplified was not the point of patentability.

Herschler is particularly on point in the present case. Like *Herschler*, applicants' invention is a method claim that has broad application to a variety of different protein markers. But the individual markers are not the invention or inventive principle of the claims. In *Herschler*, the invention was a method of passing steroids through the skin, and the claims were appropriately not limited to known steroids. Similarly, this invention is in the use of MS to detect an increase in PSA-generated markers to distinguish between prostate cancer and benign prostate hyperplasia. The fact that unknown and known markers are being detected does not detract from the patentability of the broad method claim. This is because the protein markers do not constitute the **inventive principle** underlying the claims.

In biotechnology, we often see claims that read on: (1) methods for detecting a novel protein using antibodies specific for the novel protein; (2) methods of using a novel electrophoresis gel for separating proteins; or (3) methods for treating a disease by administering a drug that does X. In each example, the inventive principle is described and enabled under §112; yet, the claims still read on *unknown* species of antibodies that bind the novel protein, *undescribed* proteins capable of being separated and *undiscovered* drugs that do X. This is the law of **inventive principle** being logically and appropriately applied to our description laws.

In view of the above legal analysis and the amendments to pending claim 1, applicants urge that the description based rejection is fully addressed and should be withdrawn.

Enablement

The Examiner rejects the claims as not enabled reminding the applicants that the description and enablement requirements are distinct requirements. In the Office Action, the Examiner urges that the claims would be enabling for specific markers but that the claims read on any markers. The eight Wands factors are cited for support. In summary, the Examiner finds the discovery of low molecular weight markers for distinguishing between prostate cancer and BPH to require undue experimentation.

Applicants respectfully remind the Examiner that the practice of the invention does not require identification of specific markers. In formal logical terms, the Examiner has supported this rejection with an "irrelevant truth." An "irrelevant truth" describes a syllogy where an accurate statement is improperly used for support of a conclusion. For example, "I am 7 foot tall; therefore, I play professional basketball."

The pending claims are directed to methods of distinguishing between prostate cancer and BPH by using MS to profile samples for low molecular weight proteins. The markers making up the profiles may be individually unidentified and require undue experimentation to identifiy. But this irrelevant truth does not mean that applicants have failed to teach how to make and use the method as claimed without undue experimentation.

The Examiner applies the Wand factors urging that the concerns raised above for description rejection also apply to the enablement requirements. Basically, the Examiner is arguing that you can't enable what you can't describe. Applicants respond as stated above for the description rejection. The non-enabled protein markers of use in the invention are not a part of the inventive principle of the claims and thus do not require enablement beyond demonstration that adequate numbers of protein are routinely detectable using MS for those to practice the claims.

The decisional law set forth above for description apply with equal force to enablement. If a hypothetical claim reads on genes defined by what they do rather than what they are structurally, that claim will fail both description and enablement aspects of §112. But the fact that it is not possible to set forth all protein markers in a given sample resulting from increased PSA activity does not render the pending claims non-enabled. Or that sample "handling" might cause problems is not a legally sufficient basis to reject the pending claims.

Any method claim is subject to this logic. For example, if we claimed a new bucket to carry water, you don't have to recite that the bucket requires gravity to function. So long as the method works as claimed using the various sample methods described with gel view type profiles, the fact that there are new and patentable protein markers to be discovered does not render the pending claims non-enabled.

Applicants are not claiming novel markers and need not enable them. The Examiner is referred to the case law on inventive principle described above for support.

Applicants remind the Examiner that this invention is more of a bio-informational-type invention and not a chemistry/composition invention. The current amendments to claim 1 are intended to address the concerns of the Examiner regarding the claims reading on using MS to detect unknown markers. It is irrelevant that there are dozens of different adjustable parameters that theoretically affect the dynamic range of any MS device for detecting low molecular weight proteins resulting from over expression of PSA.

What is relevant is that these markers are detectable using MS, and MS is a tool that does not require any express identification of specific markers because it works by mass profiles and is not focused on the primary amino acid sequences of individual markers.

The methods of profiling for low molecular weight proteins in samples using MS are well known. The "inventive principle" is in the application of well-known methods to new samples, and the methods for practice are thoroughly taught in the specification. This being true, there can be no argument that those of skill are unable to practice the invention as claimed.

Applicants believe that they have addressed all the concerns raised by the Examiner relating to enablement. Reconsideration and withdrawal of the rejection is requested in view of the comments set forth above.

PROVISIONAL DOUBLE PATENTING REJECTION

Finally, there is a provisional double patenting rejection over co-pending Application Nos. 10/221,905, 10/513,649 and 10/505,367. Applicants acknowledge the rejection and believe that the subject application will be the first to issue. Accordingly, applicants reserve the right to file a terminal disclaimer at the appropriate time during prosecution of the '905 application. Applicants believe that no further response is required (see MPEP 804 IB "Between Copending Applications - Provisional Rejections").

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance and an action to that end is respectfully requested.

Applicants believe that no fee is required for submission of this response. However if a fee is required, the Commissioner is authorized to deduct such a fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from or credit any overpayment to, the above noted Deposit Account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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